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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,761	03/10/2005	Alan Crossman	184.5USWO	3221

22462 7590 02/04/2008

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EXAMINER	
JAVANMARD, SAHAR	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
02/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,761	CROSSMAN ET AL.	
	Examiner	Art Unit	
	SAHAR JAVANMARD	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/ are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10 March 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Office Action is in response to the 371 of PCT/GB03/03801 filed March 10, 2005. Claims 1-13 have been cancelled. Newly added claims 14-26 are being examined on the merits herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for topiramate, the specification does not provide sufficient information that all compounds encompassed by the generic compound of formula I of claim 14 are capable of treating dyskinesia. Thus, the compounds encompassed by formula I of claim 14 is very broad and entails a wide array of compounds as cited in claims 14-26.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The specification does not provide sufficient information that all compounds encompassed by formula I of claim 14 are capable of treating dyskinesia.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1). The Nature of the Invention:

All of the rejected claims are drawn to an invention which pertains to a method of treating dyskinesia with the administration of a therapeutically effective amount of compounds encompassed by formula I of claim 14. The nature of the invention is complex in that it encompasses the treatment of said ailment using a wide array of compounds encompassed by formula I.

(2). Breadth of the Claims:

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass a method of treating dyskinesia with the administration of a therapeutically effective amount of compounds

encompassed by formula I. There are countless possible compounds encompassed by formula I for the treatment claimed.

(3). Guidance of the Specification:

The guidance given by the specification as to how effective the disclosed compounds are at treating the desired ailment is limited. Only biological data using topiramate is demonstrated.

(4). Working Examples:

Applicant provides examples of topiramate in a number of *in vivo* studies.

(5). State of the Art:

Levine et al. ("Medical Treatment of Essential Tremor and Parkinson's Disease", Geriatrics, 1998 May; 53(5), pages 1-10) is cited. Levine et al. states, mild essential tremor does not require treatment, and early treatment does not arrest or slow the natural progression in symptoms. When essential tremor interferes with daily activities, medical treatment options include beta-blockers, anticonvulsants, benzodiazepines, and carbonic anhydrase inhibitors. Because of the great variability in the presentation of PD, no single approach is appropriate for all patients. Levodopa is the mainstay of pharmacologic therapy for PD, although other agents are indicated for monotherapy or in combination with levodopa. These include traditional and newer dopamine agonist,

amantadine, anticholinergics, selegiline, and an emerging class of agents called COMT inhibitors." (page 1, abstract)

(6). Nature and predictability of the invention

The nature of the invention is directed towards medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(7). The Quantity of Experimentation Necessary:

In order to practice the claimed invention, one of skill in the art would have to first envision a combination of an appropriate pharmaceutical carrier, a dosage for each compound as encompassed by "formula I", the duration of treatment, route of treatment, etc. and, in the case of human treatment, an appropriate animal model system for one of the claimed compounds. One would then need to test the combination in the model system to determine whether or not the combination is effective for treating dyskinesia. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding dyskinesia treatment with any compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new

combination of the above and test the system again. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to treat dyskinesia using a compound encompassed by formula I as set forth in the claims.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, methods of treating dyskinesia by administering the various compounds of formula I of the claims are not considered to be enabled by the instant specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 23 is rejected under 3 5 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claim recites, “dyskinesia is associated with Huntington’s disease, idiopathic torsion dystonia, tardive dyskinesia. Tourette syndrome, ballista, senile chorea.” It is not clear whether the dyskinesia is associated with all these

ailments, in which case an "and" should be inserted, or if the dyskinesia is associated with one or more of these ailments, in which case an "or" should be inserted.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14-18 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Shank et al. (WO 00/61138).

Shank teaches administering compounds of formula I, namely topiramate, for treating chronic neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, Huntington's disease, multiple sclerosis, diabetic neuropathies, retinopathy, peripheral nerve injury and brain and spinal neurodegeneration arising as a result of head trauma or spinal injury (page 2, lines 6-8; claims 1-2).

In the case of Parkinson's disease, the clinical hallmarks are tremor, bradykinesia and rigidity as described by Wolters (CMAJ, 1989). Further, the onset symptoms are usually mild and vague: clumsiness of the hands, fatigue and sensory discomfort. As the disease evolves the most prominent signs appear: tremor, usually a

coarse resting tremor but one that is sometimes prominent when the patient holds a posture or performs a voluntary movement; rigidity, especially during activation of the contralateral limb; bradykinesia, associated with a disrupted pattern of fine and rapid repetitive movements (e.g., tapping and writing), lack of facial expression, diminished blinking, dysarthria, dysphagia and a slow, hesitant gait accompanied by decreased arm swing; and postural instability. Other symptoms include constipation, impotence, sialorrhea, impaired cognitive function and depression.

Thus, by administering these drugs one would inherently be treating the dyskinesia associated with these drugs, thereby meeting the limitations of claims 14-18 and 23.

Claims 14, 21, 22, and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Dursun et al. (Canadian Journal of Psychiatry, 2000).

Dursun discloses a study whereby a 29-year-old male diagnosed with chronic paranoid schizophrenia is treated with clozapine and responds positively to the medication. The patient however develops some side effects including myoclonic jerks in both hands, arms, and shoulders, in addition to excessive weight gain (column 1, paragraph 1). The same patient is then administered topiramate which showed improvement in his mood and complete improvement of his myoclonic jerks (column, paragraph 3), thus meeting the limitations of claims 14, 21, 22, and 24.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 19, 20, 25, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dursun et al. (Canadian Journal of Psychiatry, 2000) as applied to claims 14, 21, 22, and 24 above in view of Wolters et al. (CMAJ, 1989).

Dursun is discussed above. Dursun teaches treating a neurodegenerative disease with a therapeutic agent that treats the symptoms of that particular disorder,

specifically treating schizophrenia with clozapine and further administering an additional agent to treat the dyskinesia-like side effects with topiramate

Dursun does not teach the dyskinesia specifically as it applies to Parkinson's disease and further does not teach the side effect arising from dopamine replacement therapy (ie, group consisting of ropinirole, pramipexole, cabergoline, bromocriptine, lisuride, pergolide, L-DOPA and apomorphine).

Wolters teaches that L-DOPA is an effective treatment in most patients with Parkinson's disease, however, associated with L-DOPA are adverse peripheral or central reactions. Central reactions comprise of psychiatric disorders and dyskinesia (page 508-509, "Dopamine precursor" section).

It would have been obvious to one of ordinary skill in the art at the time of the invention to have used the combination therapy taught by Dursun and applied it to treating Parkinson's disease and the dyskinesia-like side effects caused by L-DOPA as taught by Wolters. L-DOPA is one of the drugs used to treat Parkinson's disease, a neurodegenerative disease like schizophrenia, and the treatment for the disease results in the same side-effect, namely dyskinesia, as taught by Wolters. Thus it would be obvious to one of ordinary skill in that art to make this substitution.

Conclusion

Claims 14-26 are not allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAHAR JAVANMARD whose telephone number is (571) 270-3280. The examiner can normally be reached on 8 AM-5 PM MON-FRI (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

SJ

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER